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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/580,711	05/18/2007	Klaus Benke	11987-00043-US	3892

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EXAMINER	
BROWE, DAVID	

ART UNIT	PAPER NUMBER
1616	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/580,711	BENKE, KLAUS	
	Examiner	Art Unit	
	DAVID M. BROWE	1616	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 February 2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *February 1, 2010*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-20 are pending; claim 21 is cancelled.

Applicants timely submission of amendments and arguments on February 1, 2010 in response to the First Office Action in the Merits is hereby acknowledged.

Priority

Applicant's claim for the benefit of prior-filed International Application No. PCT/EP04/12897, filed November 13, 2004 under 35 U.S.C. 365(c), is acknowledged. Acknowledgment is also made of applicant's claim for foreign priority under 35 U.S.C. 119(a)-(d). The certified copy has been filed in parent Application No. 10355461.0, filed in the Federal Republic of Germany on November 27, 2003.

Withdrawal of Prior Objections-Specification

The specification has been satisfactorily amended to comply with the requirements of 37 CFR 1.77(b). Therefore, the objections presented in the First Office Action are hereby withdrawn.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1-20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Straub *et al.* (U.S. Patent Application Pub. No. 20030153610), in view of Stamm *et al.* (U.S. Patent No. 6,074,670).

Applicant Claims

Applicants claim a process for the preparation of a solid, oral pharmaceutical composition comprising 5-chloro-N-({(5S)-2-oxo-3-[4-(3-oxo-4-morpholinyl)-phenyl]-1,3-oxazolidin-5-yl}-methyl)-2-thiophenecarboxamide (e.g. "active compound I") in hydrophilized form comprising a) preparing granules comprising "active compound I" in hydrophilized form by moist granulation, and b) converting the granules into the pharmaceutical composition, if appropriate with addition of pharmaceutically acceptable additives. "Active compound I" is in crystalline and micronized form, is suspended in the granulating liquid, and introduced into a fluidized bed granulation. The resulting pharmaceutical composition is a rapid-release tablet.

Applicants also claim a solid, oral pharmaceutical composition comprising "active compound I" in hydrophilized, crystalline and micronized form; sodium lauryl sulphate as a wetting agent; and hydroxypropylmethylcellulose as a hydrophilic binding agent. The "active compound I", sodium lauryl sulphate, and hydroxypropylmethylcellulose are present in a concentration of 1-60%, 0.1-5%, and 1-15%, respectively, based on the total mass. The composition is a rapid-release tablet or a tablet covered with a coating.

Applicants further claim a method for the prophylaxis and/or treatment of thromboembolic diseases comprising administering an effective amount of the pharmaceutical composition or of "active compound I" in hydrophilized form.

Determination of the Scope and Content of the Prior Art (MPEP §2141.01)

Straub *et al.* disclose a soild, oral pharmaceutical composition comprising 5-chloro-N-({(5S)-2-oxo-3-[4-(3-oxo-4-morpholinyl)-phenyl]-1,3-oxazolidin-5-yl}-methyl)-2-thiophenecarboxamide (e.g. "active compound I") (Pg. 2, sec. 0012-0018; Pg. 15, sec. 0363, 0367, 0369; Pg. 26, example 44), and a method for the prophylaxis and/or treatment of thromboembolic diseases comprising administering an effective amount of the pharmaceutical composition of "active compound I" (Pg. 1, secs. 0009-0010; Pg. 14-15, sec. 0356; Pg. 15, sec. 0364; Pg. 16, sec. 0373).

Stamm *et al.* disclose a process for the preparation of a solid, oral pharmaceutical composition comprising an active ingredient of poor aqueous solubility in hydrophilized form. In a preferred embodiment, the active ingredient is fenofibrate. The method comprises a) preparing granules comprising the active ingredient in hydrophilized form by moist granulation, and b) converting the granules into the pharmaceutical composition, if appropriate with addition of pharmaceutically acceptable additives (Col. 1, lns. 8-21, 38-63; Col. 3, lns. 32-45; Col. 4, lns. 27-28, 38-39, 60-65; Col. 5, lns. 36-67). The active ingredient is in crystalline and micronized form, is suspended in the granulating liquid, and introduced into a fluidized bed granulation (Col. 3, lns. 32-45; Col. 5, lns. 38-67). The resulting pharmaceutical composition is a rapid-release tablet (Col. 3, lns. 12-14; Col. 5, lns. 20-25).

Stamm *et al.* also disclose a solid, oral pharmaceutical composition comprising an active ingredient of poor aqueous solubility in hydrophilized, crystalline and micronized form; sodium lauryl sulphate as a wetting agent; and hydroxypropylmethylcellulose as a hydrophilic binding agent (Col. 1, lns. 10-13, 38-55; Col. 3, lns. 13-23; Col. 4, lns. 14-39; Col. 5, lns. 20-25, 29-30, 36-39). Fenofibrate is a preferred active ingredient. The active ingredient, sodium lauryl sulphate, and hydroxypropylmethylcellulose are present in a concentration of 2.5-25%, 0-5%, and 10-30%, respectively, based on the total mass including the outer phase/layer, in which the outer phase/layer is taken to comprise 50% of the total pharmaceutical composition mass (Col 4, lns. 66-67; Col. 5, lns. 1-10). The composition is a rapid-release tablet or a tablet covered with a coating (Col. 3, lns. 12-14; Col. 4, lns. 53-59; Col. 5, lns. 20-25).

Ascertainment of the Difference Between the Scope of the Prior Art and the Claims (MPEP §2141.012)

Straub *et al.* do not explicitly disclose the process of formulating and the composition containing "active compound I" in hydrophilized, crystalline and micronized form, together with sodium lauryl sulphate as a wetting agent, and hydroxypropylmethylcellulose as a hydrophilic binding agent, which can be in the form of an immediate-release tablet. This deficiency is cured by the teachings of Stamm *et al.*

Finding of Prima Facie Obviousness Rational and Motivation (MPEP §2142-2143)

It would have been *prima facie* obvious for one of ordinary skill in the art at the time of the present invention to combine the respective teachings of Straub *et al.* and Stamm *et al.* outlined *supra* to arrive at applicants claimed invention.

5-chloro-N-({(5S)-2-oxo-3-[4-(3-oxo-4-morpholinyl)-phenyl]-1,3-oxazolidin-5-yl}-methyl)-2-thiophenecarboxamide (e.g. "active compound I"), like fenofibrate, is a strongly hydrophobic, poorly water-soluble compound. Since the formulation for and the process of formulating active compounds of poor aqueous solubility disclosed by Stamm *et al.* greatly facilitated and enhanced fenofibrate's dissolution profile and bioavailability following oral administration, while alternative formulations and processes failed; one of ordinary skill in the art would be motivated to formulate "active compound I" using the Stamm *et al.* formulation and process, with the reasonable expectation that "active compound I" will exhibit a dissolution profile and bioavailability following oral administration that is likewise greatly facilitated and enhanced.

In light of the forgoing discussion, the Examiner concludes that the subject matter defined by the instant claims would have been obvious within the meaning of 35 USC 103(a).

From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Response to Arguments

Applicants claims for domestic and foreign priority have been duly acknowledged *supra*; anything stated in a previous Office Action to the contrary notwithstanding.

Applicant's arguments filed February 1, 2010 regarding the 35 USC § 103 rejection of claims 1-20 have been fully considered but they are not persuasive:

a) Applicants assert that "*Stamm et al. is concerned about fenofibrate bioavailability only*" and that "*the Patent Office does not show where Stamm et al. suggests modifying its composition or process to use another drug*". However, upon close inspection, it is clear that the Stamm *et al.* disclosure is directed generally to active ingredients of poor aqueous solubility; fenofibrate is merely a preferred embodiment. Stamm *et al.*, for example, state the following: *i)* "*The invention more particularly relates to a pharmaceutical composition for administration by oral route, containing an active ingredient of poor aqueous solubility. Numerous active ingredients suffer from the disadvantage of being poorly soluble in an aqueous medium, thus having an insufficient dissolution profile and, consequently, poor bioavailability within an organism*" (Col. 1, lns. 8-17); *ii)* "*The composition according to the invention can additionally contain any excipient conventionally used in the pharmaceutical and chemical fields which is compatible with the active ingredient*" (Col. 4, lns. 39-42); and *iii)* "*The compositions of the invention are particularly suitable for administering active ingredients by oral route*" (Col. 5, lns. 29-30). Further, Stamm *et al.* repeatedly refers to the "active ingredient(s)" throughout the disclosure.

b) Applicants assert that the Stamm *et al.* formulation/process cannot be expected to work for "active compound I" because "*Stamm et al. teaches multiple prior art references teaching fenofibrate compositions that did not solve the bioavailability problem*". However, on the contrary, it seems logical that, given all the numerous formulation/process choices available, and knowing that for any given agent some may work and other may not, one of ordinary skill in the art would be particularly motivated to try the Stamm *et al.* formulation/process for "active compound I" after it has proven successful for fenofibrate while various alternative formulations/processes have failed. Thus, in attempting to formulate a new active compound, the formulation chemist would do well to first try formulations/processes proven successful before those shown previously to fail.

c) Applicants assert that "*Neither Stamm et al. nor Straub et al. suggested the importance of hydrophilization to improve bioavailability in the absence of improvement in dissolution*". However, applicants are not claiming a composition or a process exhibiting improved bioavailability in the absence of improvement in dissolution.

Applicant's amendment necessitated the modified ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not

mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Inquiries

Any inquiry concerning this communication or earlier communications from the examiner should be directed to DAVID M. BROWE whose telephone number is 571-270-1320. The examiner can normally be reached on Monday-Friday 7:30AM-5PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Johann R. Richter can be reached on 571-272-0646. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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